REMARKS

Claims 6, 8, 9, and 19-23 are pending and under examination. Claims 1-5, 7, and 10-18 were canceled previously. In the present amendment, Applicants amend claims 6, 8, and 19-22 as described below. Applicants acknowledge, with appreciation, the Office's withdrawal of all previous objections and rejections and removal of finality. Action at page 2.

Claims 6, 8, 19, and 22 have each been amended to recite ". . . test stem cell, test stem cell tissue, or test stem cell nucleus. . . ." Those amendments merely make explicit what was previously implicit in the claim language. No new matter has been added. In addition, claims 8, 20, 21, and 22 have each been amended to recite ". . . stem cell, stem cell tissue, or stem cell nucleus. . . ." Those amendments also merely make explicit what was previously implicit in the claim language. No new matter has been added. Finally, claim 19 has been amended to recite "[t]he method of claim 8, wherein the test stem cell, test stem cell tissue, or test stem cell nucleus is an embryonic stem cell, embryonic stem cell tissue, or embryonic stem cell nucleus." Those amendments promote claim consistency and, as stated above, merely make explicit what was previously implicit in the claim language. No new matter has been added.

I. Rejection of Claims 6, 8, 9, and 19-23 Under 35 U.S.C. § 103(a)

The Office newly rejected claims 6, 8, 9, and 19-23 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Olek et al. (U.S. Patent No. 6,214,556) in view of Ohgane et al., Dev. Gen. 22:132-140 (1998) further in view of Labosky et al., Development 120:3197-3204 (1994). Applicants respectfully traverse the rejection.

The Office alleged that the "[t]he instant claims are drawn to a method of identifying the differentiation state of a stem cell by comparing the methylation pattern of a stem cell to the methylation pattern of a cell of a known differentiation state." Action at page 3. The Office

further alleged that "Olek et al. teaches a generic method of identifying cell types as well as cell states or stages through the use of methylation fingerprint patterns." *Id.* The Office also alleged that "Ohgane et al. provide 'differentiation state-specific DNA methylation patterns' that distinguished the placenta from kidney." *Id.* Finally, the Office alleged that "Labosky et al. provide the methylation patterns of embryonic germ cell lines (undifferentiated cells), embryonic stem cell lines, and compare the patterns of methylation of the embryonic germ cell lines and the embryonic stem cell lines." *Id.* at page 4. The Office then concludes that "[o]ne of ordinary skill in the art at the time the invention was made would have combined the methods of Olek et al. with Ohgane et al. and Labosky et al. to create a method of identifying unknown cell samples." *Id.* at page 5. Moreover, the Office alleges that the combination teaches the limitations of claim 8. *Id.* at page 4.

Applicants respectfully disagree. Applicants assert that the Office has failed to establish a *prima facie* case of obviousness. As set forth in the M.P.E.P. at § 2143 at page 2100-129, three basic criteria must be met:

> First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Applicants assert that none of the documents, either alone or in combination, teach or suggest all the limitations of either independent claim 8 or independent claim 22. For example, none of the documents, either alone or in combination, teach or suggest "obtaining a differentiation state-specific DNA methylation pattern for one or more stem cell, stem cell tissue, or stem cell nucleus of known differentiation state," as recited in independent claim 8. Nor do any of the documents, either alone or in combination, teach or suggest "obtaining a cell-, tissue-,

or nucleus-specific DNA methylation pattern for one or more known types of stem cell, stem cell tissue, or stem cell nucleus," as recited in independent claim 22.

The Office acknowledged that Olek et al. "do not specifically teach using a reference pattern for differentiation states to determine the differentiation state of a stem cell [and] do not teach the instant claims as they are specifically applied to differentiation states." Action at page 3. Ohgane et al. does not cure the deficiencies of Olek et al. According to the Office, "Ohgane et al. provide 'differentiation state-specific DNA methylation patterns' that distinguished the placenta from kidney." *Id.* But Ohgane et al. is silent regarding "a differentiation state-specific DNA methylation pattern for one or more stem cell, stem cell tissue, or stem cell nucleus of known differentiation state," as well as "a cell-, tissue-, or nucleus-specific DNA methylation pattern for one or more known types of stem cell, stem cell tissue, or stem cell nucleus."

Labosky et al. fails to cure the deficiencies of Ohgane et al. and Olek et al. Labosky et al. studied "the methylation state of the putative imprinting box of the maternally expressed insulin-like growth factor 2 receptor (*Igf2r*) gene . . . in different EG cell lines, . . . normal somatic cells and ES cells." Labosky at page 3198. Labosky et al. discusses certain results in Fig. 2. (p. 3201) and Table 3 (p. 3200). Labosky et al. states that "[h]alf of the 8.5 days p.c. derived EG cell lines (9 out of 18) . . . [show a] pattern of methylation [that] is characteristic of somatic cells and 5 different pluripotent ES cell lines. . . . The remaining [EG] cell lines . . . have a different pattern of methylation. . . ." *Id.* at page 3200 (references to tables, figures, and named cell lines omitted). Since Labosky et al. shows that the methylation pattern of half of the EG cell lines is "characteristic of somatic cells and 5 different pluripotent ES cell lines," while the methylation pattern of the other half of EG cell lines is "different," it clearly does not teach or suggest "a differentiation state-specific DNA methylation pattern for one or more stem cell,

stem cell tissue, or stem cell nucleus." For at least the same reasons, Labosky et al. similarly does not teach or suggest "a cell-, tissue-, or nucleus-specific DNA methylation pattern for one or more known types of stem cell, stem cell tissue, or stem cell nucleus."

Not only does Labosky et al. fail to teach or suggest the claimed methods, it actually teaches away from them. For example, Labosky et al. discusses that certain methylation patterns are shared between embryonic cells at two different stages of development (EG cells and ES cells) and somatic cells (terminally-differentiated fibroblasts). Labosky at page 3200. Thus, those results demonstrate a methylation pattern that is neither "differentiation state-specific" nor "cell-, tissue-, or nucleus-specific." As a further example, Labosky et al. demonstrates that half of the EG cell lines have a certain methylation pattern, while the other half has a different methylation pattern. *Id.* Thus, EG cells do not have a methylation pattern that one skilled in the art would recognize as "differentiation state-specific" or "cell-, tissue-, or nucleus-specific." Nowhere does Labosky et al. teach or suggest such "differentiation state-specific" or "cell-, tissue-, or nucleus-specific" methylation patterns. Indeed, the results discussed above, as well as the demonstrated methylation heterogeneity and methylation instability of the EG cell lines (*see, e.g.*, Table 3, Figs. 2 and 3) teach away from "a differentiation state-specific DNA methylation pattern for one or more stem cell, stem cell tissue, or stem cell nucleus" and "a cell-, tissue-, or nucleus-specific DNA methylation pattern for one or more known types of stem cell, stem cell tissue, or stem cell nucleus."

Because Labosky et al. teaches away from the claimed invention, as discussed above, one skilled in the art would not be motivated to combine Labosky et al. with Olek et al. and Ohgane et al. Moreover, based on the results of Labosky et al., one skilled in the art would not have a reasonable expectation of success of obtaining "a differentiation state-specific DNA methylation

pattern for one or more stem cell, stem cell tissue, or stem cell nucleus," or of obtaining "a cell-, tissue-, or nucleus-specific DNA methylation pattern for one or more known types of stem cell, stem cell tissue, or stem cell nucleus," as taught by the present inventors.

Thus, for at least these reasons, the Office has failed to establish a *prima facie* case of obviousness. Accordingly, independent claims 8 and 22 would not have been obvious in view of Olek et al., and Ohgane et al., and further in view of Labosky et al, nor would dependent claims 6, 9, 19-21, and 23 have been obvious. Therefore, Applicants respectfully request reconsideration and withdrawal of the rejection of claims 6, 8, 9, and 19-23 under 35 U.S.C. § 103(a) as allegedly being unpatentable over Olek et al. in view of Ohgane et al., further in view of Labosky et al.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of the application and the timely issuance of a Notice of Allowance. If the Examiner does not consider the claims allowable, the undersigned requests that, prior to taking action, the Examiner call her at (650) 849-6749 to set up an interview.

Please grant any extensions of time required to enter this response and charge any additional required fees to Deposit Account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

Dated: June 6, 2006

By: _____
Jennifer L. Davis
Reg. No. 54,632
Customer No. 22,852